Clinical features and outcomes of the membraneous glomerulonephritis associated with rheumatoid arthritis: an observational study.

Oyama A[1] and Matsushima H[2]

[1]Nephrology Division, Nishikobe Medical Center, Kobe City Hospital Organization, Kobe, JAPAN; [2]Matsushima Clinic, Kobe, JAPAN

Kobe City Hospital Organization

INTRODUCTION AND OBJECTIVES: Rheumatoid arthritis is an important situation in relation with the membraneous glomerulonephritis, especially in the cases which are treated by bucillamine. Discontinuation of bucillamine is believed to improve proteinuria of the bucillamine-induced membraneous nephropathy, however, the outcomes of bucillamine-induced membraneous glomerulonephritis are not fully ellucidated. In this study, in order to illustrate the relation between treatment and outcomes of rheumatoid arthritis-related membraneous glomerulonephritis, we investigated the patient background, treatment and outcome of these patients and compared with idiopathic membraneous glomerulonephritis.

METHODS: Our analysis include 12 consecutive patients with both rheumatoid arthritis and biposy-proven membraneous glomerulonephritis, who were diagnosed in the years between 2004 and 2015 in our center (group 1). In 9 patients, bucillamine was still administered when renal biopsy was performed, 2 patients were taken biopsy after discontinuation of bucillamine, and remaining 1 patient had never been administered bucillamine nor suspicious drugs that may cause membraneous glomerulonephritis. Group 2 includes 53 consequent idiopathic membraneous glomerulonephritis patients, who were taken biopsies in the same period (Table 1). A urinary protein concentration was evaluated as gram per gram creatinine (g/gCr), and a glomerular filtration ratio (GFR) was estimated by using the revised equation for estimated GFR by Japanese Society of Nephrology (Figure 1). In this study, urinary protein concentration, estimated GFR, blood pressure and treatments were recorded up to 5 years for investigation.

CONCLUSION: Although some patients associated with bucillamine required corticosteroids because of heavy proteinuria, the majority of patients showed proteinuria reduction after discontinuation of bucillamine without any imunosuppressive therapy. Probablly due to small sample size, there was no significant difference between groups, however, proteinuria reduction seemed to be more drastic, and better outcome may be expected, in bucillamine-associated patients than idiopathic patients.

$$eGFR = 194 \times Cr^{-1.094} \times Age^{-0.287} \ (\times 0.739 \ if \ female) \ mL/min \cdot 1.73 \ m^2$$

Cr: serum creatinine, Age: year-old

Figure 1. Revised equation for estimated GFR by Japanese Society of Nephrology

Table 1: Baseline Patient Characteristics

	Group 1 (n = 12)	Group 2 (n = 53)	P
Age (year-old)	61.4 ± 16.6	64.8 ± 5.4	0.14
Gender (M : F)	(3 : 9)	(40 : 13)	0.03
Urinary protein (g/gCr)	8.10 ± 2.96	8.92 ± 5.16	0.73
eGFR (mL/min•1.73 m²)	63.8 ± 31.2	71.1 ± 14.9	0.82
Systolic blood pressure (mmHg)	128 ± 15	132 ± 21	0.77
Diastolic blood pressure (mmHg)	75 ± 11	79 ± 13	0.82

Table 2: Patient characteristics of rheumatoid arthritis cases.

Age (year-old)	Gender	duration of bucillamine (months)	maximum prednisolone (mg/day)	remarks	yearly urinary protein (g/gCr)						yearly eGFR (mL/min•1.73 m2)					
					year 0	1	2	3	4	5	year 0	1	2	3	4	5
73	f	7	30	died in year 0	11.32	n/a	n/a	n/a	n/a	n/a	47.0	n/a	n/a	n/a	n/a	n/a
56	m	6	20		8.15	0.21	0.32	0.25	0.19	0.39	68.6	77.6	60.5	65.2	67.2	53.7
35	f	8	never		4.72	0.82	0.35	0.11	0.15	0.28	66.0	59.0	63.2	53.4	56.9	50.3
67	f	9	20		8.03	1.21	0.57	0.82	1.54	1.02	116.9	82.1	77.2	83.1	78.0	73.5
70	f	6	never		3.31	0.18	0.38	0.29	0.51	0.88	52.6	55.4	48.3	46.4	49.80	45.49
40	f	6	40	moved in year 4	7.13	3.80	2.13	1.26	n/a	n/a	101.7	91.3	89.0	76.7	n/a	n/a
84	f	4	never		12.90	0.13	0.27	1.58	0.88	1.51	26.0	26.5	25.3	23.6	21.2	22.0
75	m	never	never		9.17	2.39	0.31	0.48	0.61	0.77	23.6	37.9	33.6	31.1	28.9	26.0
53	f	14	never		8.14	2.44	0.52	0.76	0.58	0.81	72.3	70.7	60.4	61.9	64.4	53.4
64	m	7	never		9.51	6.84	2.41	1.14	1.05	1.49	47.7	61.9	57.7	56.8	64.1	60.9
53	f	5	never		7.35	3.88	1.84	0.71	0.82	0.66	54.8	52.5	50.3	53.9	51.7	55.5
67	f	9	never		7.47	1.53	0.58	0.52	1.17	1.39	89.0	69.2	65.3	78.6	71.3	75.0

RESULTS: In bucillamine administrered patients, mean administration period before the appearance of massive proteinuria was 6.8 months. One patient in group 1 died 4 months after renal biopsy due to interstitial pneumonia, and another patient could not observe after year 4 due to house moving. Four patients in group 1 (33 %) were administered prednisone (20-40 mg/day), and 45 patients in group 2 (85 %) were administered prednisolone or some immunosuppressive agents. Proteinuria level at the biopsy was 8.10±2.96 g/gCr in group 1, and 8.92±5.16 g/gCr in group 2. With patients who had been followed up more than 3 years, proteinuria level at year 3 was 0.72±0.61 g/gCr in group 1 (n = 11) and 1.87 ± 3.57 in group 2 (n = 44) (Figure 2). Mean estimated GFR was 63.84±31.24 and 71.14±14.94 mL/min•1.73 m² at baseline, and 57.34±23.13 and 64.09±17.52 mL/min•1.73 m² at year 3, respectively (Fugure 3). There was significant decrease of proteinuria level in both groups, however, no significant change was observed in eGFR. There was also no significant difference between groups. There was also no significant difference of blood pressure between groups and between years (data not shown).
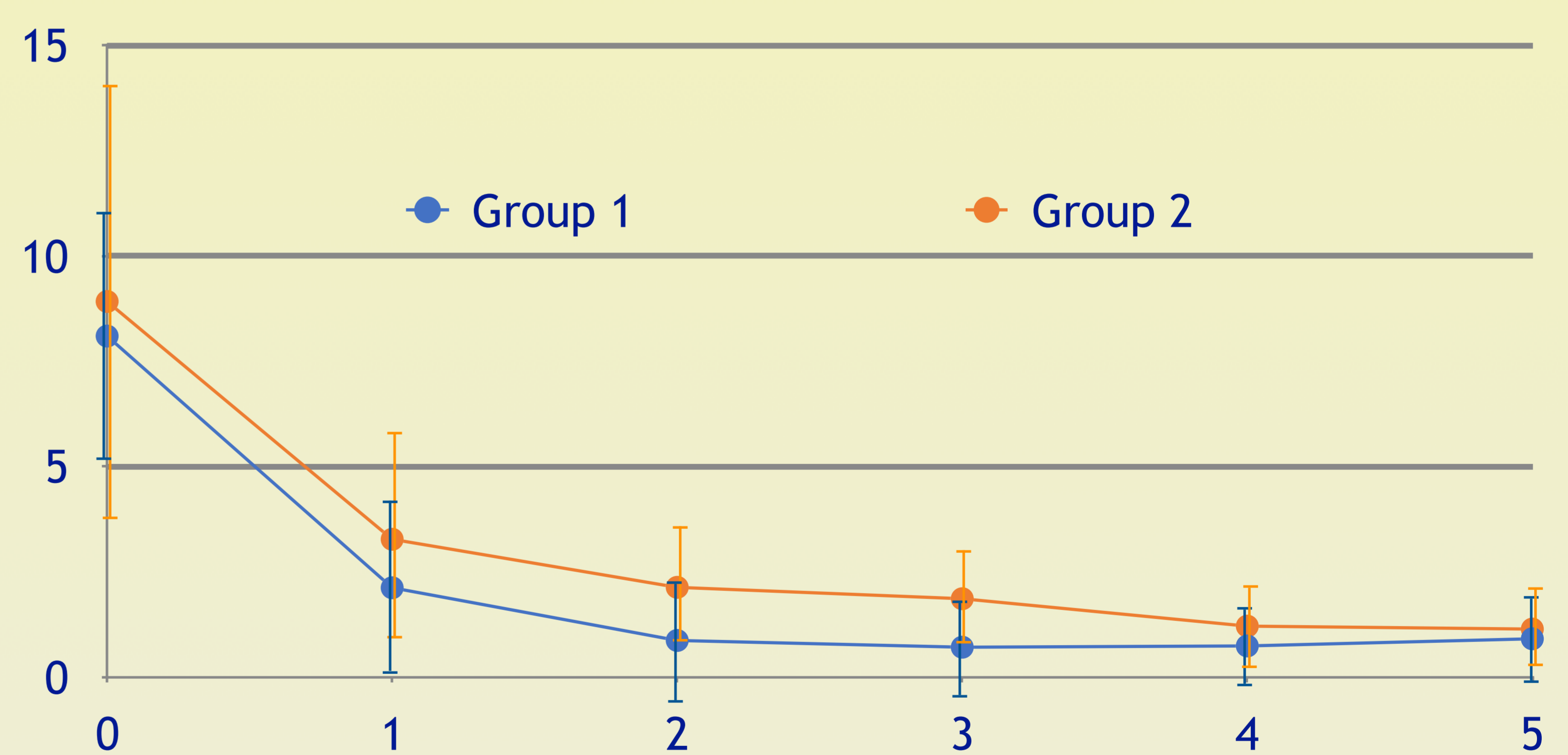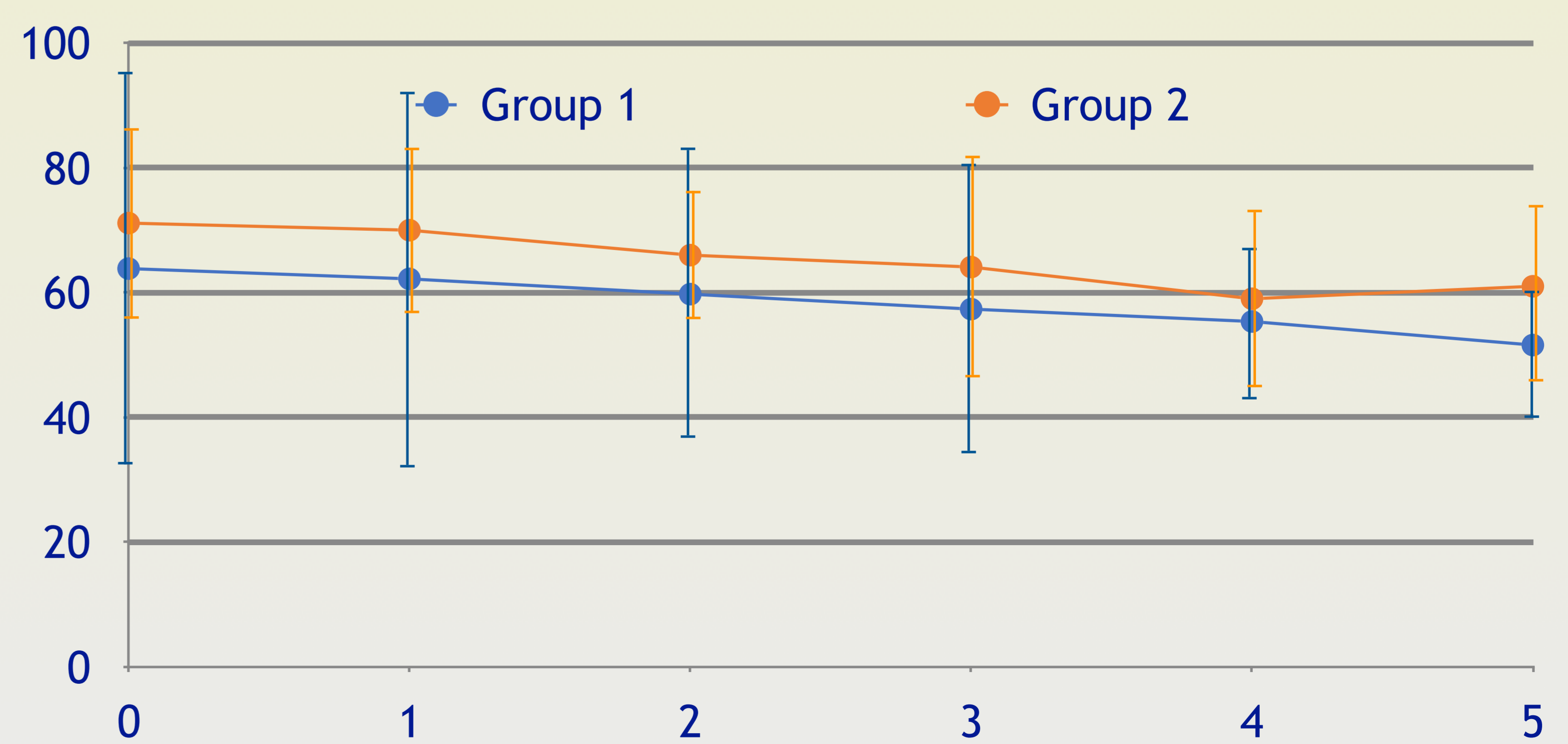

Figure 2: Yearly concentration of urinary protein

Figure 3: Yearly estimated glomerular filtration ratio

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